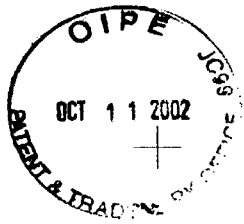




1 / 25

1 CGGCAGCAAAGGAACGTGCGAACGCGTGACGCCGCCCGACTGGCTCGCGCTCTCCCGTGC
61 CCCGGCGTCCTCCGCCCCGCTCATGGCCCCGGGCCGCCGCGGACGAGCGGCGCTGAGGCGGG
121 CCGCGTGAGACGTGAGGCGGCCGCCGTGGCCCTCACAGTCGGCGTTTCGCCGCCTGCC
181 GCGGTGCCCGCGCACGCCTGCCGCCATCGCCTTCGCGCTGGCTGGCGGGGGCGCTGTCC
241 TCCCAGGCCGTCCGCGCCGCTCCCTGGAGCTCGGCGGAGCGCGGCAGCCAGGGCCGGCGG
301 AGGCGCGAGGAGCCGGGCGCCACCGCCGCCGCCGCCGCCGCCGCCGGGGGCCATGACC
361 GTGGAGCAGAACGTGCTGCAGCAGAGCGCGGCGCAGAAGCACCAGCAGACGTTTTTGAAT
421 CAACTGAGAGAAATTACGGGGATTAATGACACCCAGATACTACAGCAAGCCTTGAAGGAT
481 AGTAATGGAACTTGAATTAGCAGTGGCTTTCTTACTGCGAAGAATGCTAAGACCCCT
541 CAGCAGGAGGAGACAACTTACTACCAAACAGCACTTCTTGGCAATGATAGATACATCAGT
601 GTGGGAAGCCAAGCAGATACAAATGTGATTGATCTCACTGGAGATGATAAAGATGATCTT
661 CAGAGAACAATTGCCTTGAGTTTGGCCGAATCAAACAGGGCATTTCAGGGAGACTGGAATA
721 ACTGATGAGGAACAAGCCATTAGCAGAGTTCTTGAAGCCAGTATAGCAGAGAATAAAGCA
781 TGTTTGAAGAGGACACCTACAGAAGTTTGGAGGGATTCTCGAAACCCTTATGATAGAAAA
841 AGACAGGACAAAGCTCCCGTTGGGCTAAAGAATGTTGGCAATACTTGTGTTGGTTTAGTGCT
901 GTTATTCAGTCATTATTTAATCTTTTGAATTTAGAAGATTAGTTCTGAATTACAAGCCT
961 CCATCAAATGCTCAAGATTTACCCCGAAACCAAAGGAACATCGGAATTTGCCTTTTATG
1021 CGTGAGCTGAGGTATCTATTTGCACTTCTTGTGTTGGTACCAAAGGAAGTATGTTGATCCA
1081 TCAAGAGCAGTTGAAATTTCTTAAGGATGCTTTCAAATCAAATGACTCACAGCAGCAAGAT
1141 GTGAGTGAGTTTACACACAAATTATTAGATTGGTTAGAAGATGCCTTCCAAATGAAAGCT
1201 GAAGAGGAGACGGATGAAGAGAAGCCAAAGAACCCCATGGTAGAGTTGTTCTATGGCAGA
1261 TTCCTGGCTGTGGGAGTACTTGAAGGTAAAAAATTTGAAAACACTGAAATGTTTGGTCAG
1321 TACCCACTTCAGGTCAATGGGTTCAAAGATCTGCATGAGTGCCTAGAAGCTGCAATGATT
1381 GAAGGAGAAATTGAGTCTTTACATTACAGAGAATTCAGGAAAATCAGGCCAAGAGCATTGG
1441 TTTACTGGATTACCACCTGTGTTAACATTTGANTTGTCAAGATTTGAATTTAATCAGGCA
1501 TTGGGAAGACCAGAAAAAATTCACAACAAATTAGAATTTCCCCAAGTTTTATATTTGGAC
1561 AGATACATGCACAGAAACAGAGAAATAACAAGAATTAAGAGGGAAGAGATCAAGAGACTG
1621 AAAGATTACCTCACGGTATTACAACAAAGGCTAGAAAGATATTTAAGCTATGGTTCCGGT
1681 CCCAAACGATTCCCCTTGGTAGATGTTCTTCAGTATGCATTTGGAATTTGCCTCAAGTAAA
1741 CCTGTTTGCACCTTCTCCTGTTGACGATATTGACGCTAGTTCCCCACCTAGTGGTTCCATA
1801 CCATCACAGACATTACCAAGCACAAACAGAACAACAGGGAGCCCTATCTTCAGAACTGCCA
1861 AGCACATCACCTTCATCAGTTGCTGCCATTTTCATCGAGATCAGTAATACACAAACCATT
1921 ACTCAGTCCCGGATACCTCCAGATTTGCCCATGCATCCGGCACCAAGGCACATAACGGAG
1981 GAAGAACTTTCTGTGCTGGAAAGTTGTTTACATCGCTGGAGGACAGAAATAGAAAATGAC
2041 ACCAGAGATTTGCAGGAAAGCATATCCAGAATCCATCGAACAATTGAATTAATGTACTCT
2101 GACAAATCTATGATACAAGTTCCTTATCGATTACATGCCGTTTTTAGTTTCACGAAGGCCAA
2161 GCTAATGCTGGGCACTACTGGGCATATATTTTTTGATCATCGTGAAAGCAGATGGATGAAG
2221 TACAATGATATTGCTGTGACAAAATCATCATGGGAAGAGCTAGTGAGGGACTCTTTTGGT
2281 GGTATAGAAATGCCAGTGCATACTGTTTAATGTACATAAATGATAAGGCACAGTTCCTA
2341 ATACAAGAGGAGTTTAATAAAGAACTGGGCAGCCCCCTTGTGTTGGTATAGAAACATTACCA
2401 CCGGATTTGAGAGATTTTGTGAGGAAGACAACCAACGATTTGAAAAAGAACTAGAAGAA
2461 TGGGATGCACAACCTGCCCAGAAAGCTTTGCAGGAAAAGCTTTTAGCGTCTCAGAAATTG
2521 AGAGAGTCAGAGACTTCTGTGACAACAGCACAAGCAGCAGGAGACCCAGAATATCTAGAG
2581 CAGCCATCAAGAAGTGATTTCTCAAAGCACTTGAAAGAAGAACTATTCAAATAATTACC
2641 AAGGCATCACATGAGCATGAAGATAAAAGTCCTGAAACAGTTTTTGAGTCGGCAATTAAG
2701 TTGGAATATGCAAGGTGGTTAAGTTGGCCCAAGAAGACACCCACCAGAAACCGATTAT
2761 CGTTTACATCATGTAGTGGTCTACTTTATCCAGAACCAGGCACCAAAGAAAATTATTGAG
2821 AAAACATTACTAGAACAAATTTGGAGATAGAAATTTGAGTTTTGATGAAAGGTGTCACAAC
2881 ATAATGAAAGTTGCTCAAGCCAACTGGAAATGATAAAACCTGAAGAAGTAACTTGGAG
2941 GAATATGAGGAGTGGCATCAGGATTATAGGAAATTCAGGGAAACAACCTATGTATCTCATA

FIG._1A



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3001 ATTGGGCTAGAAAATTTTCAAAGAGAAAGTTATATAGATTTCCTTGCTGTTCCATCTGT
3061 GCTTATCAGAATAACAAAGAACTCTTGCTTAAAGGCTTATACAGAGGACATGATGAAGAA
3121 TTGATATCACATTATAGAAGAGAATGTTTGCTAAATTAATGAGCAAGCCGCAGAACTC
3181 TTCGAATCTGGAGAGGATCGAGAAGTAAACAATGGTTTGATTATCATGAATGAGTTTATT
3241 GTCCCATTTTTTGCCATTATTACTGGTGGATGAAATGGAAGAAAAGGATATACTAGCTGTA
3301 GAAGATATGAGAAATCGATGGTGTTCCTACCTTGGTCAAGAAATGGAACCACACCTCCAA
3361 GAAAAGCTGACAGATTTTTTGCCAAAACCTGCTTGATTGTTCTATGGAGATTAAAAGTTTC
3421 CATGAGCCACCGAAGTTACCTTCATATTCCACGCATGAACTCTGTGAGCGATTGCCCCGA
3481 ATCATGTTGTCCCTCAGTCGAACTCCTGCTGATGGAAGATTAAACTGCACACTTTCCCTGA
3541 ACACACTGTATAAACTCTTTTTAGTTCTTAACCCTTGCCTTCCTGTCACAGGGTTTGCTT
3601 GTTGCTGCTATAGTTTTTAACTTTTTTTTTATTTTAATAACTGCAAAAGACAAAATGACTA
3661 TACAGACTTTAGTCAGACTGCAGACAATAAAGCTGAAAATCGCATGGCGCTCAGACATTT
3721 TAACCGGAAGTGTATATAATCACAAATCTAATTGATTTTATTATGGCAAACTATGCTT
3781 TTGCCACCTTCCTGTTGCAGTATTACTTTGCTTTTATCTTTTCTTCTCAACAGCTTTCC
3841 ATTCAGTCTGGATCCTTCCATGACTACAGCCATTTAAGTGTTTCAGCACTGTGTACGATAC
3901 ATAATATTTGGTAGCTTGTAATGAAATAAAGAATAAAGTTTTATTATGGCTAC

FIG._1B

1 MTVEQNVLQQSAAQKHQQTFLNQLREITGINDTQILQQALKDSNGNLELAVAFLTAKNAK
61 TPQQEETTYYYQTALPGNDRIYSVGSQADTNVIDLTGDDKDDLQRTIALSLAESNRAFRET
121 GITDEEQAISRVLEASIAENKACLKRTPTFVWRDSRNPYDRKRQDKAPVGLKNVGNTCWF
181 SAVIQSLFNLLFRRLVLNYKPPSNAQDLPRNQKEHRNLPFMRELRYLFALLVGTKRKYV
241 DPSRAVEILKDAFKSNDSQQQDVSEFTHKLLDWLEDAFQMKAEETDEEKPKNPMVELFY
301 GRFLAVGVLEGKKFENTEMFGQYPLQVNGFKDLHECLEAAMIEGEIESLHSENSGKSGQE
361 HWFTGLPPVLTFXLRSFEFNQALGRPEKIHNKLEFPQVLYLDHYMHRNREITRIKREEIK
421 RLKDYLTVLQQRLERYLSYSGPKRFPPLVDVLQYALEFASSKPVCTSPVDDIDASSPPSG
481 SIPSQTLPTSTTEQQGALSSELPSTSPSSVAAISSRSVIHKPFTQSRIPPDLPMPAPRHI
541 TEEELSVLESLHRWRTEIENDTRDLQESISRIHRTIELMYSDKSMIQVPYRLHAVLVHE
601 GQANAGHYWAYIFDHRESRWMKYNDIAVTKSSWEELVRDSFGGYRNASAYCLMYINDKAQ
661 FLIQEEFNKETGQPLVGIETLPPDLRDFVEEDNQRFEEKELEEWDAQLAQKALQEKLLASQ
721 KLRESESVTTAQAGDPEYLEQPSRSDFSKHLKEETIQIITKASHEHEDKSPETVLQSA
781 IKLEYARLVKLAQEDTPPETDYRLHHVVVYFIQNQAPKKIIEKTLLEQFGDRNLSFDERC
841 HNIMKVAQAKLEMIKPEEVNLEEYEEWHQDYRKFRETTMYLIIGLENFQRESYIDSLLFL
901 ICAYQNNKELLSKGLYRGHDEELISHYRRECLLKLNEQAALFESGEDREVNGLIIMNE
961 FIVPFLPLLLVDEMEEKDILAVEDMRNRWC SYLGQEMEPHLQEKLTDFLPKLLDCSMEIK
1021 SFHEPPKLPSYSTHELCECFARIMLSLSRTPADGR

FIG._2





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1 CGGCAGCAAAGGAACGTGCGAACGCGTGACGCCGCCCGACTGGCTCGCGCTCTCCCGTGC
61 CCCGGCGTCTCTCCGCCCGCTCATGGCCCCGGGCCCGCCGCGGACGAGCGGCGCTGAGGCGGG
121 CCGCGTGAGACGTGAGGCGGCCCGCCGTGGCCCTCACAGTCGGCGTTTCGCCGCTTGCCC
181 GCGGTGCCCGCGCACGCCTGCCGCCATCGCCTTCGCGCCTGGCTGGCGGGGGCGCTGTCC
241 TCCCAGGCCGTCCGCGCCGCTCCCTGGAGCTCGGCGGAGCGCGGCAGCCAGGGCCGGCGG
301 AGGCGCGAGGAGCCGGGCGCCACCGCCGCCGCCGCCGCCGCCGCCGGGGGCCATGACC
361 GTGGAGCAGAACGTGCTGCAGCAGAGCGCGGCGCAGAAGCACCAGCAGACGTTTTTGAAT
421 CAACTGAGAGAAATTACGGGGATTAATGACACCCAGATACTACAGCAAGCCTTGAAGGAT
481 AGTAATGGAACTTGGAATTAGCAGTGGCTTTCCTTACTGCGAAGAATGCTAAGACCCCT
541 CAGCAGGAGGAGACAACCTTACTACCAAACAGCACTTCCTGGCAATGATAGATACATCAGT
601 GTGGGAAGCCAAGCAGATACAAATGTGATTGATCTCACTGGAGATGATAAAGATGATCTT
661 CAGAGAACAATTGCCTTGAGTTTGGCCGAATCAAACAGGGCATTACAGGGAGACTGGAATA
721 ACTGATGAGGAACAAGCCATTAGCAGAGTTCTTGAAGCCAGTATAGCAGAGAATAAAGCA
781 TGTTTGAAGAGGACACCTACAGAAGTTTGGAGGGATTCTCGAAACCCTTATGATAGAAAA
841 AGACAGGACAAAGCTCCCGTTGGGCTAAAGAATGTTGGCAATACTTGTGTTGTTTAGTGCT
901 GTTATTCAAGTCATTATTTAATCTTTTGAATTTAGAAGATTAGTTCTGAATTACAAGCCT
961 CCATCAAATGCTCAAGATTTACCCCGAAACCAAAGGAACATCGGAATTTGCCTTTTATG
1021 CGTGAGCTGAGGTATCTATTTGCACTTCTTGTGTTGGTACCAAAGGAAGTATGTTGATCCA
1081 TCAAGAGCAGTTGAAATTCTTAAGGATGCTTTCAAATCAAATGACTCACAGCAGCAAGAT
1141 GTGAGTGAGTTTACACACAAATTATTAGATTGGTTAGAAGATGCCTTCCAAATGAAAGCT
1201 GAAGAGGAGACGGATGAAGAGAAGCCAAAGAACCCCATGGTAGAGTTGTTCTATGGCAGA
1261 TTCCTGGCTGTGGGAGTACTTGAAGGTAAGGTAAGGTAAGGTAAGGTAAGGTAAGGTAAGG
1321 TACCCACTTCAGGTCAATGGGTTCAAAGATCTGCATGAGTGCCTAGAAGCTGCAATGATT
1381 GAAGGAGAAATTGAGTCTTTACATTACAGAGAATTCAGGAAAATCAGGCCAAGAGCATTGG
1441 TTTACTGGATTACCACCTGTGTTAACATTTGANTTGTCAAGATTTGAATTTAATCAGGCA
1501 TTGGGAAGACCAGAAAAAATTCACAACAAATTAGAATTTCCCAAGTTTTATATTTGGAC
1561 AGATACATGCACAGAAACAGAGAAATAACAAGAATTAAGAGGGAAGAGATCAAGAGACTG
1621 AAAGATTACCTCACGGTATTACAACAAAGGCTAGAAAGATATTTAAGCTATGGTTCCGGT
1681 CCCAAACGATTCCCCTTGGTAGATGTTCTTCAGTATGCATTGGAATTTGCCTCAAGTAAA
1741 CCTGTTTGCACCTTCTCCTGTTGACGATATTGACGCTAGTTCCCCACCTAGTGGTTCCATA
1801 CCATCACAGACATTACCAAGCACAAACAGAAACAACAGGGAGCCCTATCTTCAGAACTGCCA
1861 AGCACATCACCTTCATCAGTTGCTGCCATTTTCATCGAGATCAGTAATACACAAACCATTT
1921 ACTCAGTCCCGGATACCTCCAGATTTGCCCATGCATCCGGCACCAAGGCACATAACGGAG
1981 GAAGAACTTTCTGTGCTGGAAAGTTGTTTACATCGCTGGAGGACAGAAATAGAAAATGAC
2041 ACCAGAGATTTGCAGGAAAGCATATCCAGAATCCATCGAACAATTGAATTAATGTACTCT
2101 GACAAATCTATGATACAAGTTCCTTATCGATTACATGCCGTTTTAGTTTACGAAGGCCAA
2161 GCTAATGCTGGGCACTACTGGGCATATATTTTTGATCATCGTGAAAGCAGATGGATGAAG
2221 TACAATGATATTGCTGTGACAAAATCATCATGGGAAGAGCTAGTGAGGGACTCTTTTGGT
2281 GGTATAGAAATGCCAGTGCATACTGTTTAATGTACATAAATGATAAGGCACAGTTCCTA
2341 ATACAAGAGGAGTTTAATAAAGAAACTGGGCAGCCCCCTTGTGGTATAGAAACATTACCA
2401 CCGGATTTGAGAGATTTTGTGAGGAAGACAACCAACGATTTGAAAAAGAACTAGAAGAA
2461 TGGGATGCACAACCTTGCCCAGAAAGCTTTGCAGGAAAAGCTTTTAGCGTCTCAGAAATTG
2521 AGAGAGTCAGAGACTTCTGTGACAACAGCACAAAGCAGCAGGAGACCCAGAATATCTAGAG
2581 CAGCCATCAAGAAGTGATTTCTCAAAGCACTTGAAAGAAGAACTATTCAAATAATTACC
2641 AAGGCATCACATGAGCATGAAGATAAAAGTCCTGAAACAGTTTTTGCAGTCGGCAATTAG
2701 TTGGAATATGCAAGGTTGGTTAAGTTGGCCCAAGAAGACACCCACCAGAAACCGATTAT
2761 CGTTTACATCATGTAGTGGTCTACTTTATCCAGAACCAGGCACCAAAGAAAATTATTGAG
2821 AAAACATTACTAGAACAAATTTGGAGATAGAAATTTGAGTTTTGATGAAAGGTGTCACAAC
2881 ATAATGAAAGTTGCTCAAGCCAAACTGGAAATGATAAAACCTGAAGAAGTAACTTGGAG
2941 GAATATGAGGAGTGGCATCAGGATTATAGGAAATTCAGGGAAACAACCTATGTATCTCATA

FIG._3A



3001 ATTGGGCTAGAAAATTTTCAAAGAGAAAGTTATATAGATTCCCTTGCTGTTCCCTCATCTGT
3061 GCTTATCAGAATAACAAAGAACTCTTGCTCTAAAGGCTTATACAGAGGACATGATGAAGAA
3121 TTGATATCACATTATAGAAGAGAATGTTTGCTAAT**CCTTTAATTTAAAAAGGAAACAAAAA**
3181 **CCTATTCTTTTTTTTTTTCCTGCATTGCATTAAAGAAATTAATGAGCAAGCCGCAGAACTC**
3241 TTCGAATCTGGAGAGGATCGAGAAGTAAACAATGGTTTGATTATCATGAATGAGTTTATT
3301 GTCCCATTTTTTGCCATTATTACTGGTGGATGAAATGGAAGAAAAGGATATACTAGCTGTA
3361 GAAGATATGAGAAATCGATGGTGTTCCTACCTTGGTCAAGAAATGGAACACACCTCCAA
3421 GAAAAGCTGACAGATTTTTTGCCTAACTGCTTGATTGTTCTATGGAGATTAAAAGTTTC
3481 CATGAGCCACCGAAGTTACCTTCATATTCACGCATGAACCTCTGTGAGCGATTGCCCCGA
3541 ATCATGTTGTCCCTCAGTCGAACCTCTGCTGATGGAAGAT**TAA**ACTGCACACTTTCCTGA
3601 ACACACTGTATAAACTCTTTTTAGTTCTTAACCCTTGCCCTTCCTGTACAGGGTTTGCTT
3661 GTTGCTGCTATAGTTTTTAACTTTTTTTTATTTTAATAACTGCAAAAGACAAAATGACTA
3721 TACAGACTTTAGTCAGACTGCAGACAATAAAGCTGAAAATCGCATGGCGCTCAGACATTT
3781 TAACCGAACTGATGTATAATCACAAATCTAATTGATTTTATTATGGCAAAACTATGCTT
3841 TTGCCACCTTCCTGTTGCAGTATTACTTTGCTTTTATCTTTTCTTCTCAACAGCTTTC
3901 ATTCAGTCTGGATCCTTCCATGACTACAGCCATTTAAGTGTTTACGACTGTGTACGATAC
3961 ATAATATTTGGTAGCTTGTAATGAAATAAAGAATAAAGTTTTATTTATGGCTAC

FIG._3B

1 MTVEQNVLQQSAAQKHQQTFLNQLREITGINDTQILQQALKDSNGNLELAVAFLTAKNAK
61 TPQQEETTYQYQTALPGNDRIISVGSQADTNVIDLTGDDKDDLQRTIALSLAESNRAFRET
121 GITDEEQAISRVLEASIAENKACLKRTPTFVWRDSRNPYDRKRQDKAPVGLKNVGNTCWF
181 SAVIQSLFNLLFRRLVLNYKPPSNAQDLPRNQKEHRNLPFMRELRYLFALLVGTKRKYV
241 DPSRAVEILKDAFKSNDSSQQQDVSEFTHKLLDWLEDAFQMKAEETDEEKPKNPMVELFY
301 GRFLAVGVLEGKKFENTEMFGQYPLQVNGFKDLHECLEAAMIEGEIESLHSENSGKSGQE
361 HWFTGLPPVLTFXLRFEFNQALGRPEKIHNLKLEFPQVLYLDHYMHRNREITRIKREEIK
421 RLKDYLTVLQQLRLERYLSYSGPKRFPLVDVLQYALEFASSKPVCTSPVDDIDASSPPSG
481 SIPSQTLPTSTTEQQGALSSELPSTSPSSVAAISSRSVIHKPFTQSRIPPDLPMHPAPRHI
541 TEEELSVLESCLHRWRTEIENDTRDLQESISRIHRTIELMYSKSMIQVPYRLHAVLVHE
601 GQANAGHYWAYIFDHRESRWMKYNDIAVTKSSWEELVRDSFGGYRNASAYCLMYINDKAQ
661 FLIQEEFNKETGQPLVGIETLPPDLRDFVEEDNQRFKEKELEEWDAQLAQKALQEKLLASQ
721 KLRESETSVTTAQAAAGDPEYLEQPSRSDFSKHLKEETIQIITKASHEHEDKSPETVLQSA
781 IKLEYARLVKLAQEDTPPETDYRLHHVVVYFIQNQAPKKIIEKTLLEQFGDRNLSFDERC
841 HNIMKVAQAKLEMIKPEEVNLEEYEEWHQDYRKFRETTMYLIIGLENFQRESYIDSLLFL
901 ICAYQNNKELLSKGLYRGHDEELISHYRRECLLILNLKRKQKPIFFFLHCIKKLNEQAA
961 ELFESGEDREVNGLIIMNEFIVPFLPLLLVDEMEEKDILAVEDMRNRWCSYLGQEMEPH
1021 LQEKLTDFLPKLLDCSMEIKSFHEPPKLPSYSTHELCELFARIMLSLSRTPADGR

FIG._4





mtSUP Suppresses α -IgM Induced NFAT-Luciferase Activity as a Dominant-negative Mutant

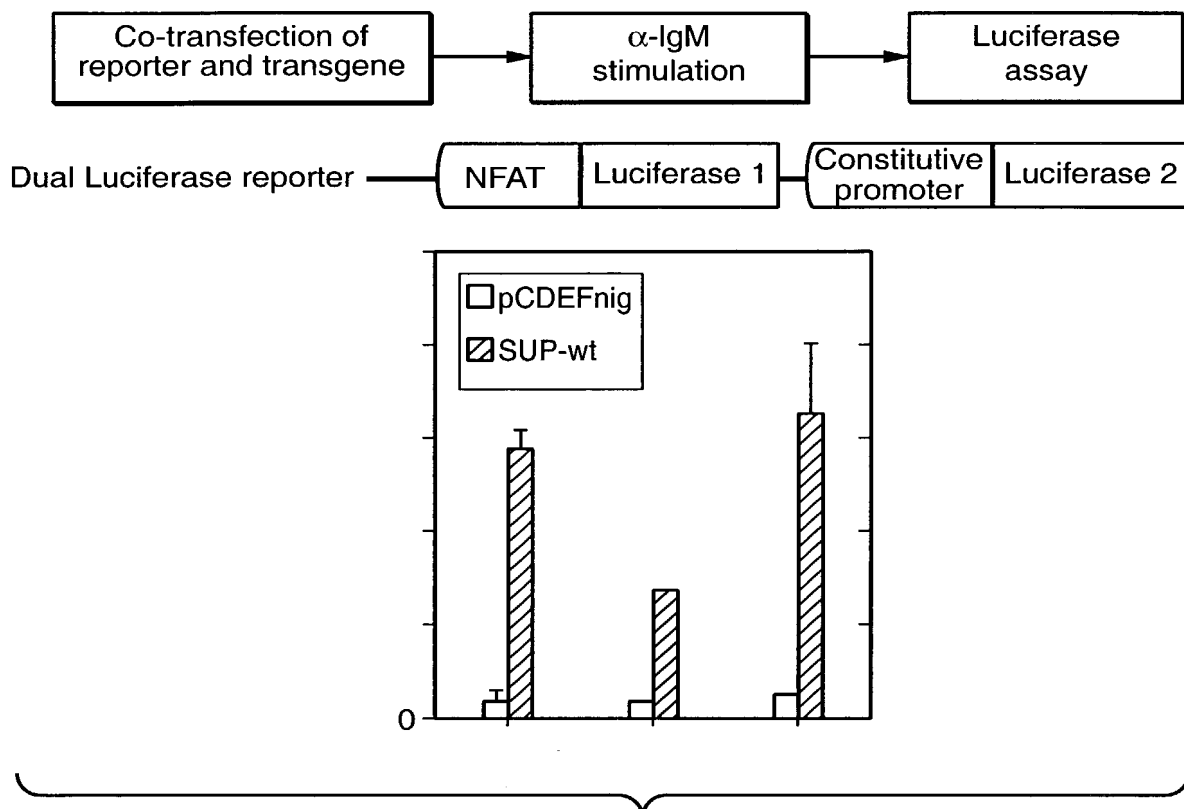


FIG._6

Model: SUP Regulates BCR Signaling by Stabilizing Syk

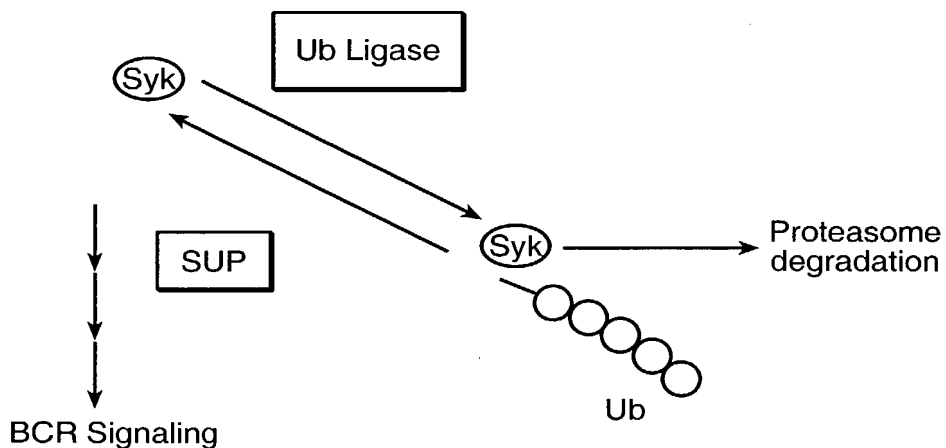


FIG._7





YTH Screen Using Syk as Bait: Hits Likely Encode the
Regulatory Domain of USP-25 (SUP)

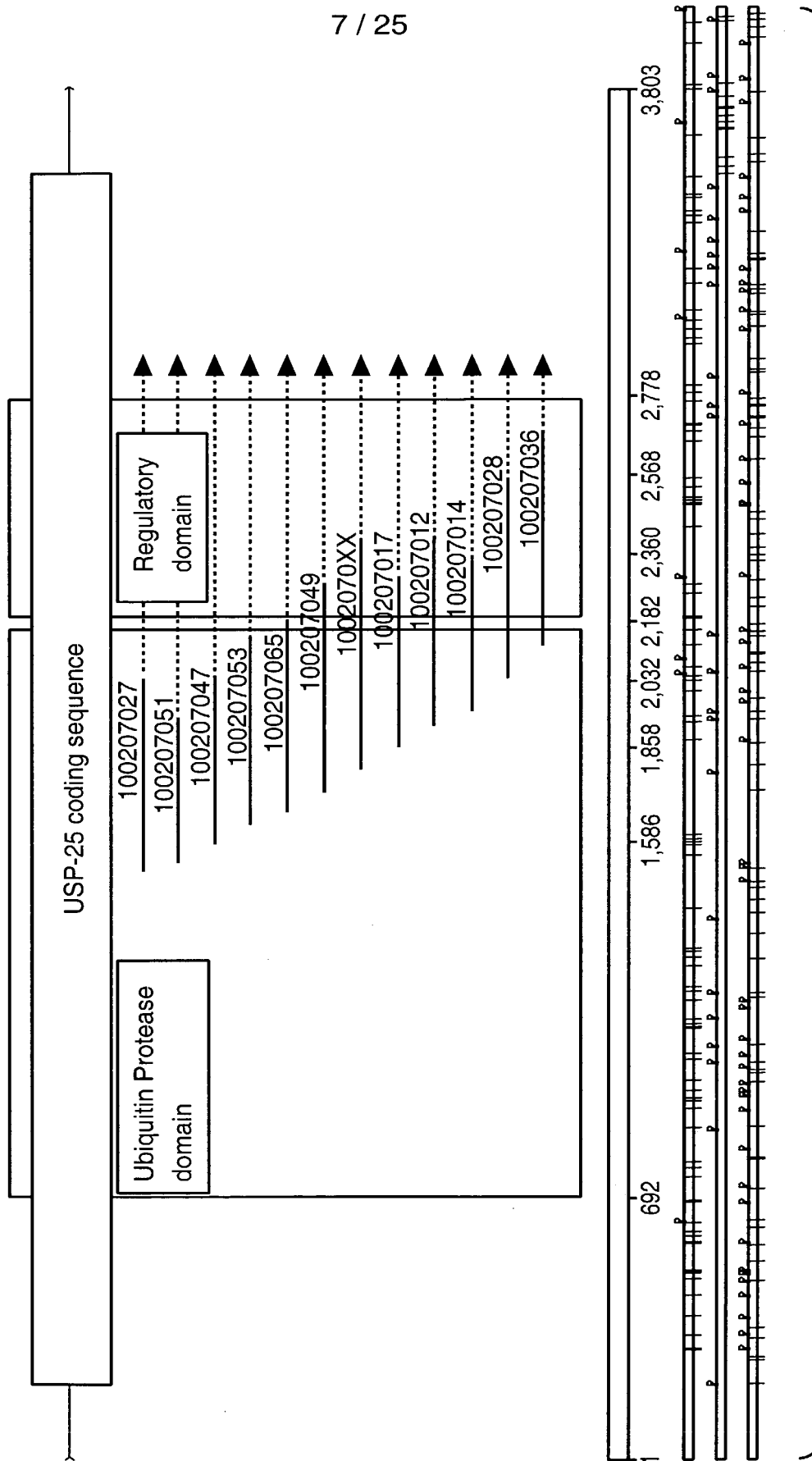


FIG._8



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USP-25 mRNA Expression Profile

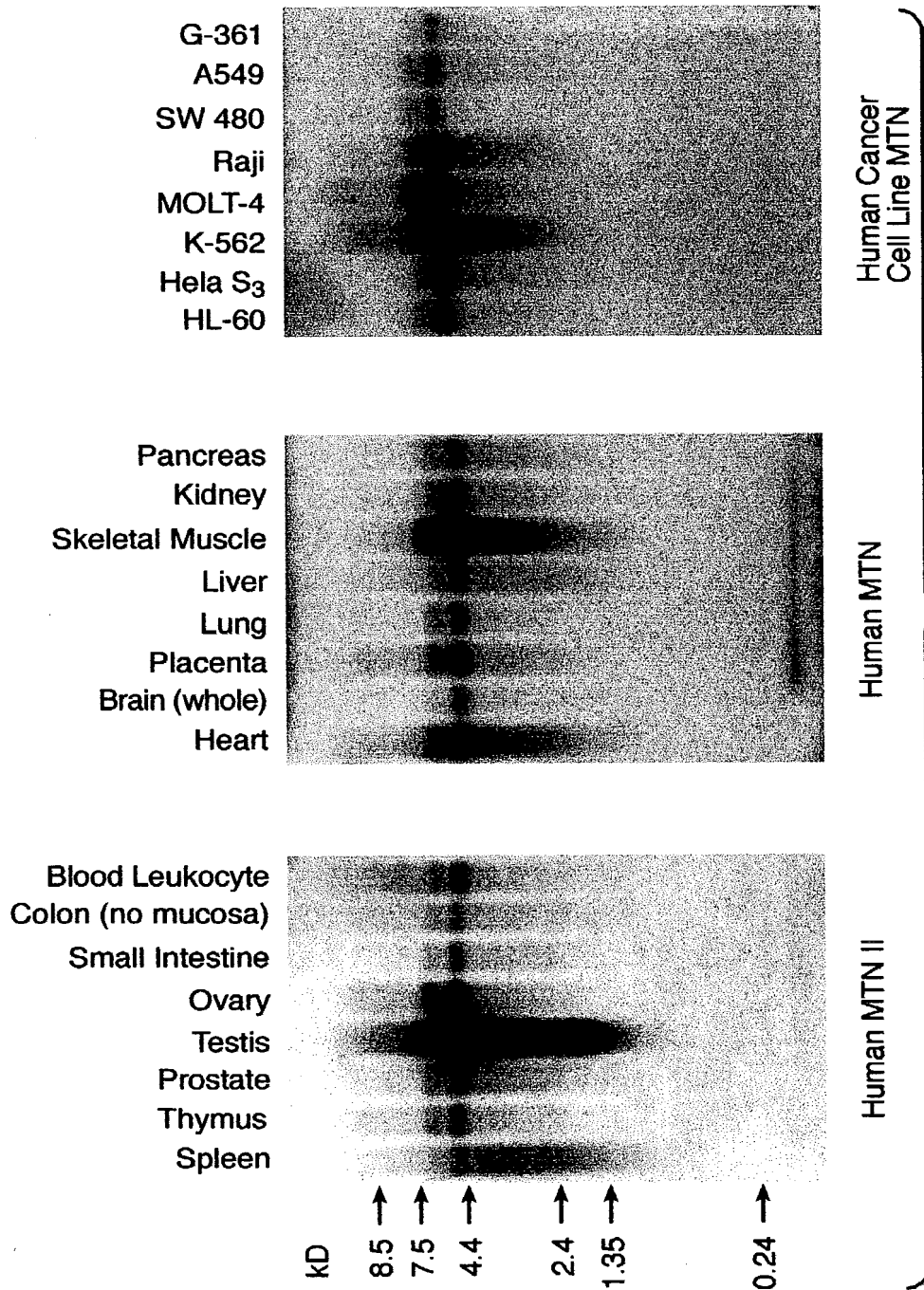


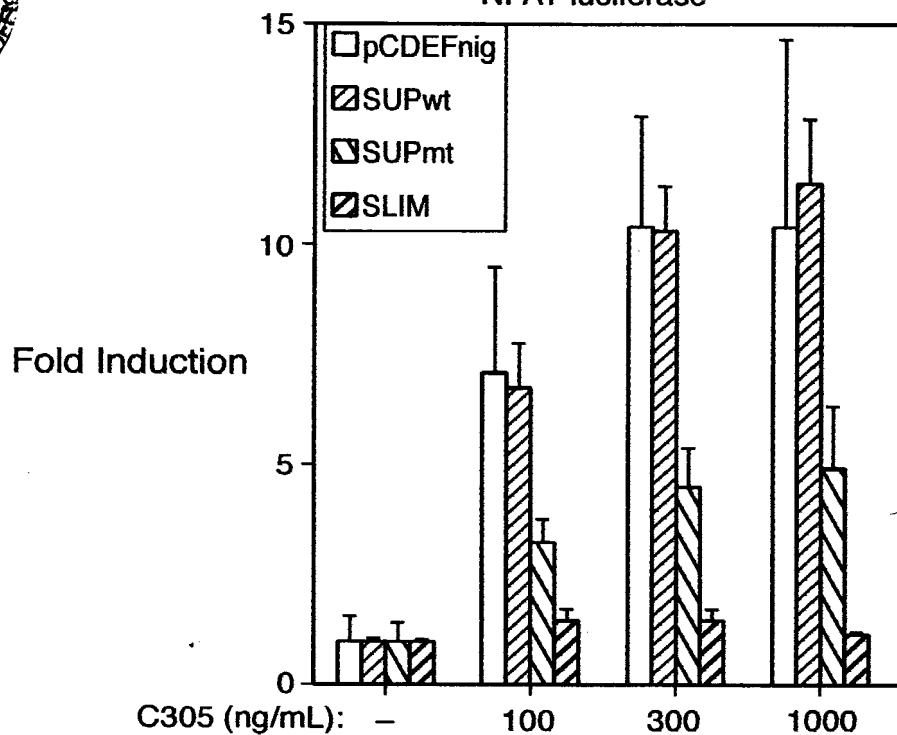
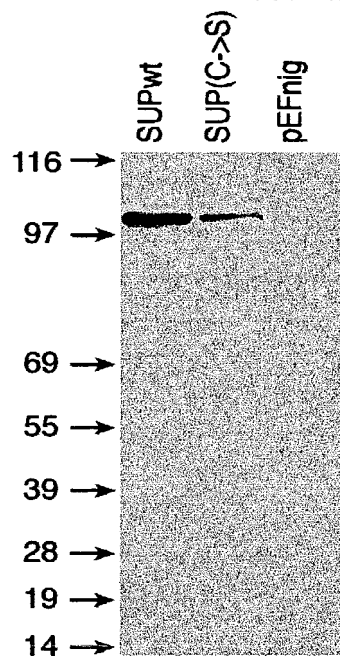
FIG. 9B

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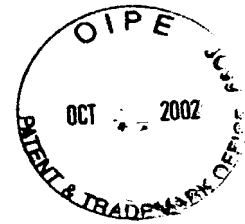
**Catalytically Inactive USP-25(C->S)
Blocks TCR-Induced NFAT Activity**

NFAT-luciferase

**FIG. 10A****Catalytically Inactive USP-25(C->S)
Blocks TCR-Induced NFAT Activity**

wb: anti-FLAG

FIG. 10B



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**Catalytically Inactive USP-25
Inhibits Downstream TCR Signaling**

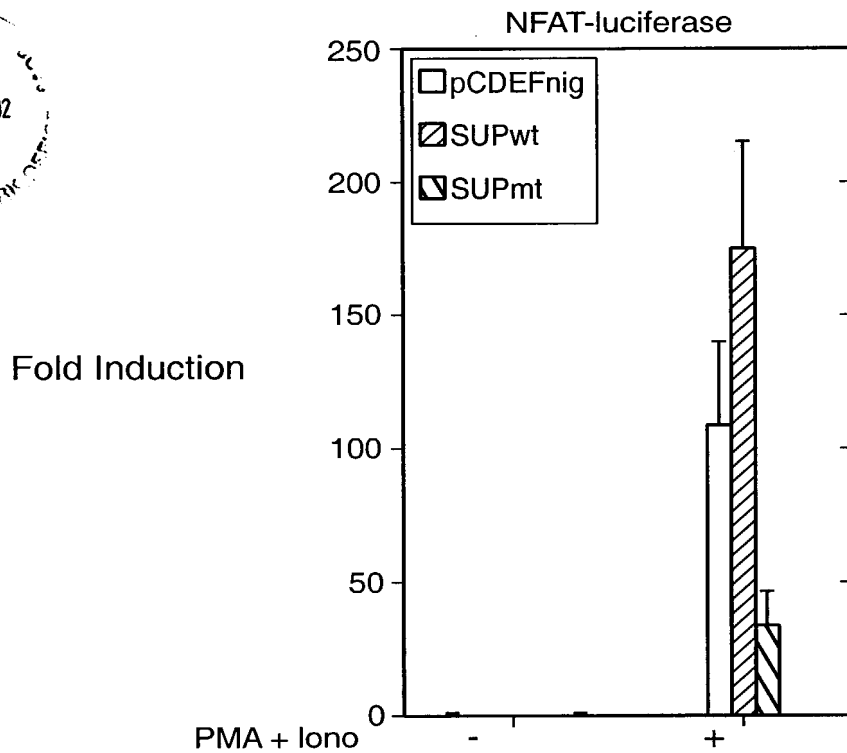
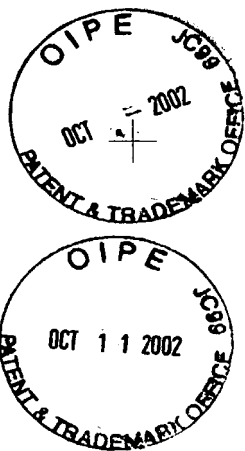


FIG. 10C

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Catalytically Inactive USP-25(C->S) Does Not Affect AP-1 Activity

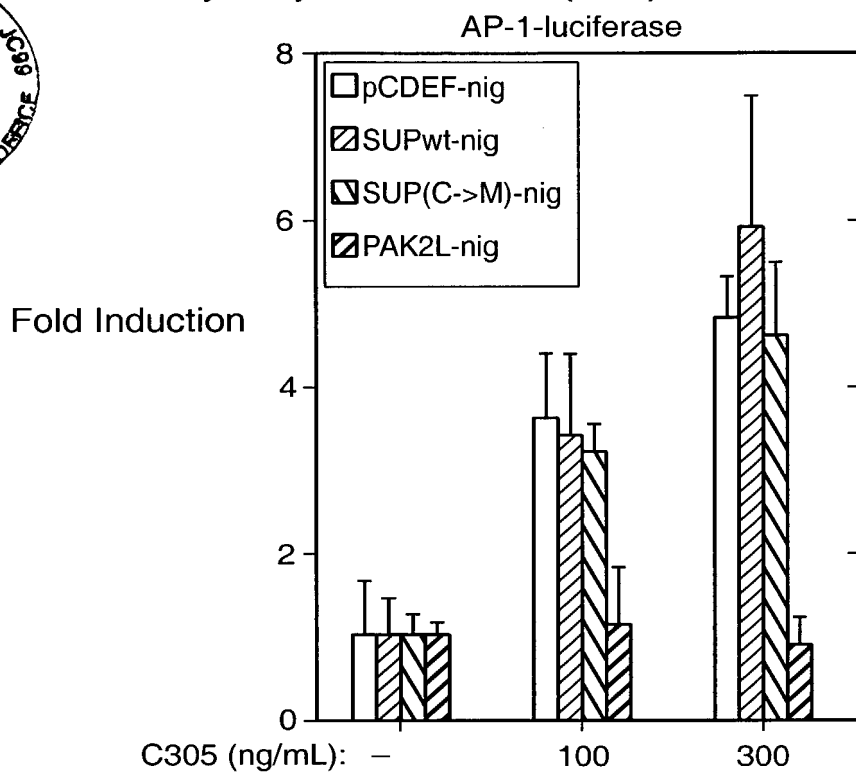


FIG._11A

Catalytically Inactive USP-25(C->S) Does Not Affect AP-1 Activity

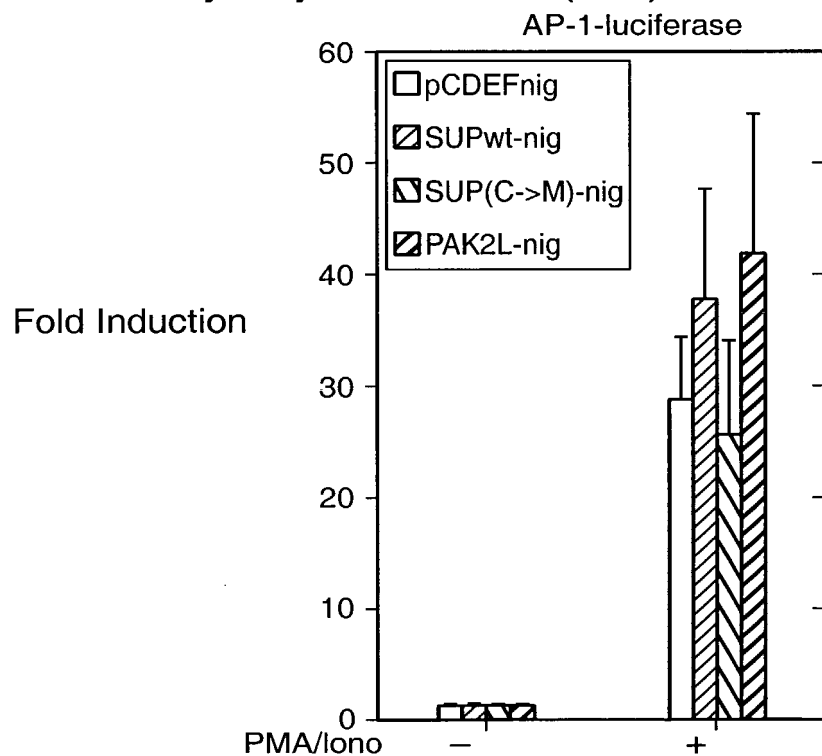


FIG._11B





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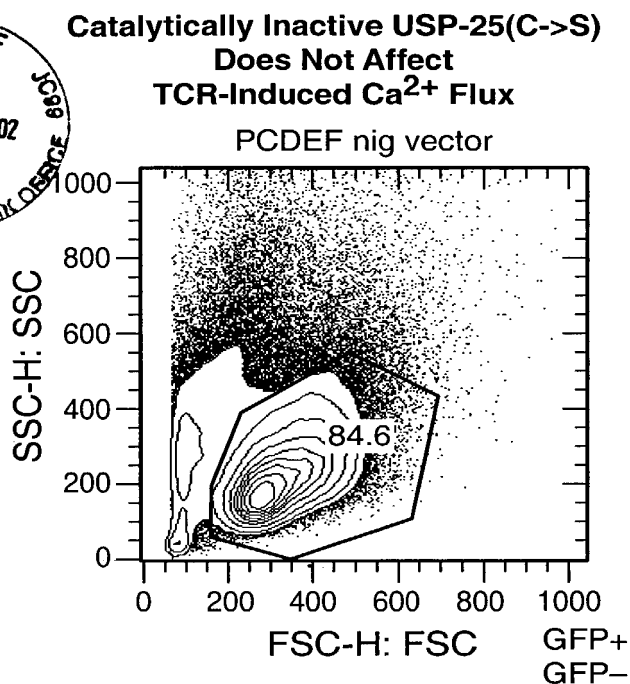


FIG._11C

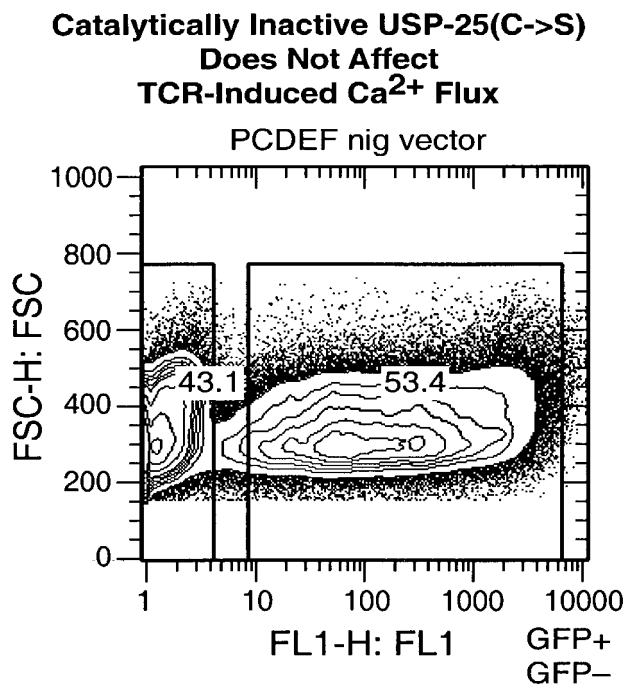


FIG._11D

**Catalytically Inactive USP-25(C->S)
Does Not Affect TCR-Induced Ca^{2+} Flux**

PCDEF nig vector

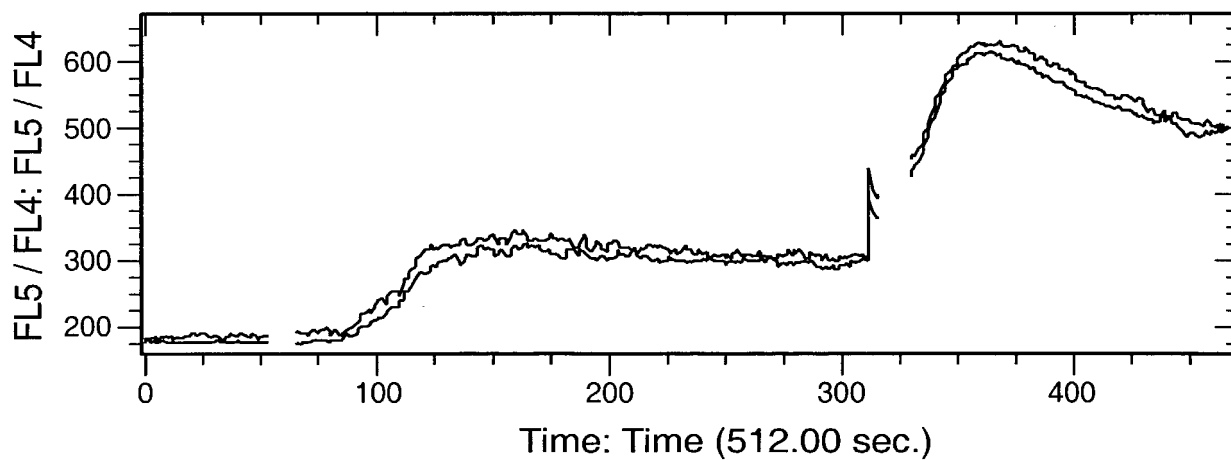


FIG._11E





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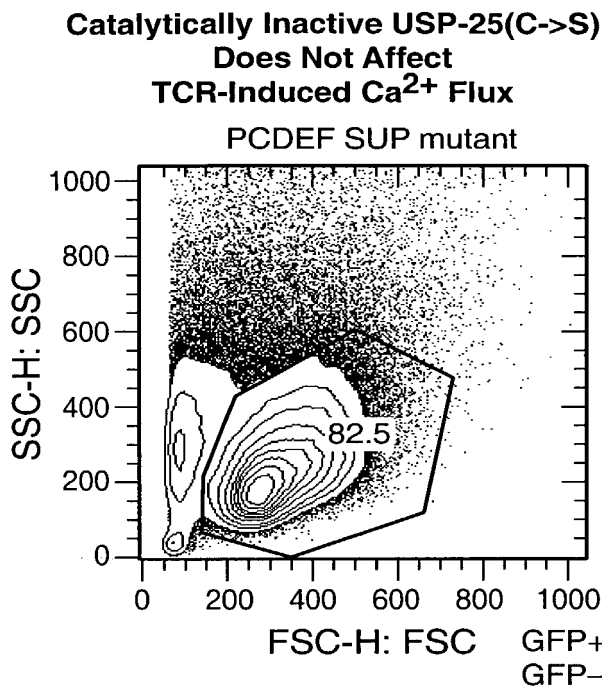


FIG._11F

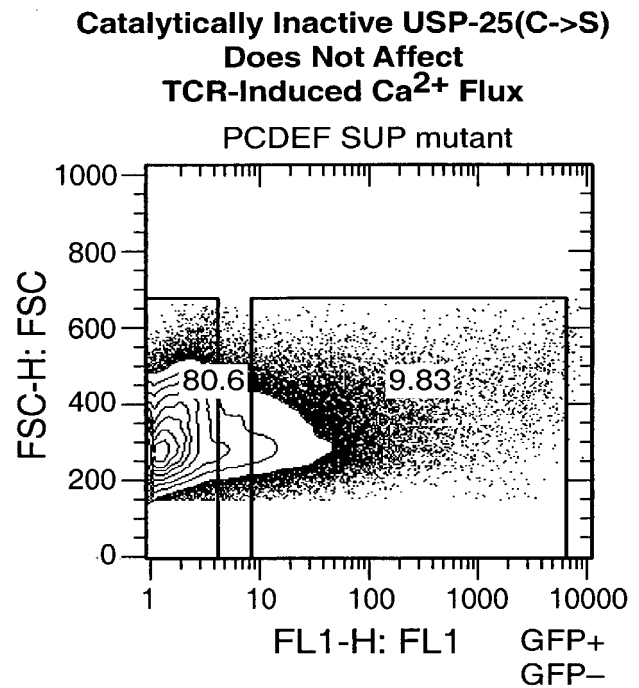


FIG._11G

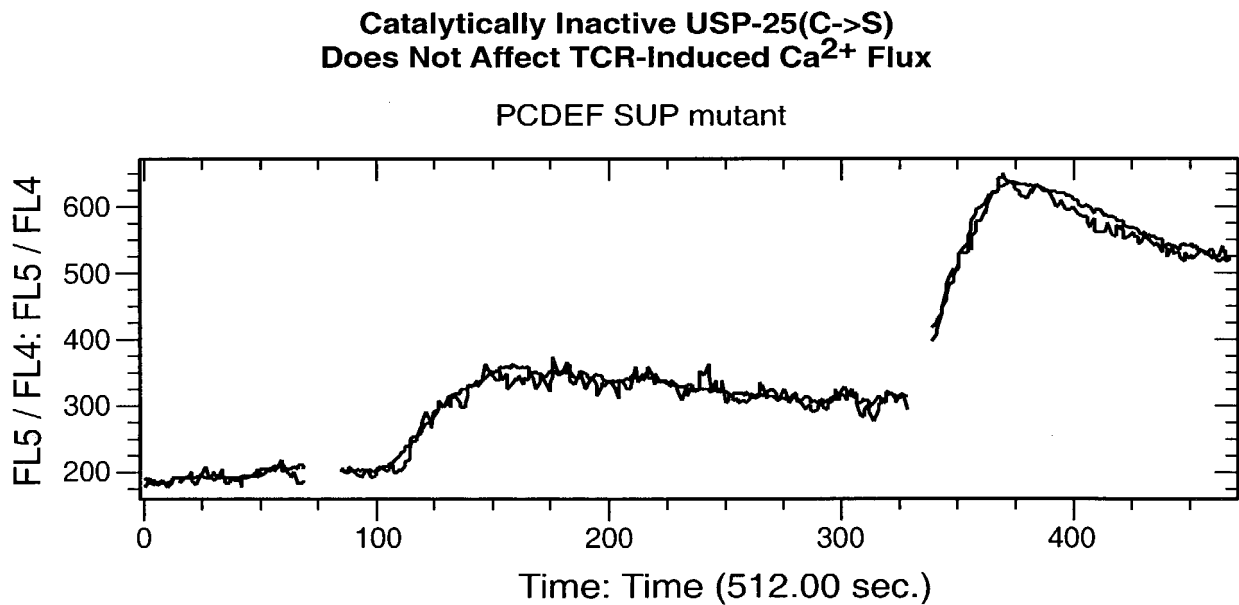


FIG._11H





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**Catalytically Inactive USP-25(C->S)
Does Not Affect
TCR-Induced Ca^{2+} Flux**

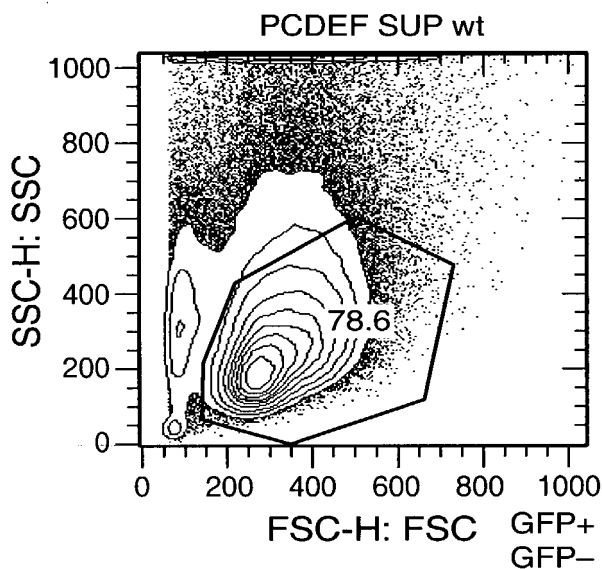


FIG._11I

**Catalytically Inactive USP-25(C->S)
Does Not Affect
TCR-induced Ca^{2+} Flux**

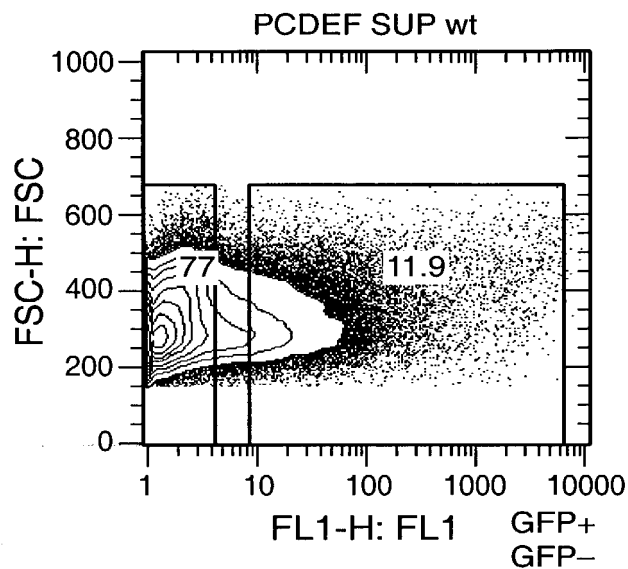


FIG._11J

**Catalytically Inactive USP-25(C->S)
Does Not Affect TCR-Induced Ca^{2+} Flux**

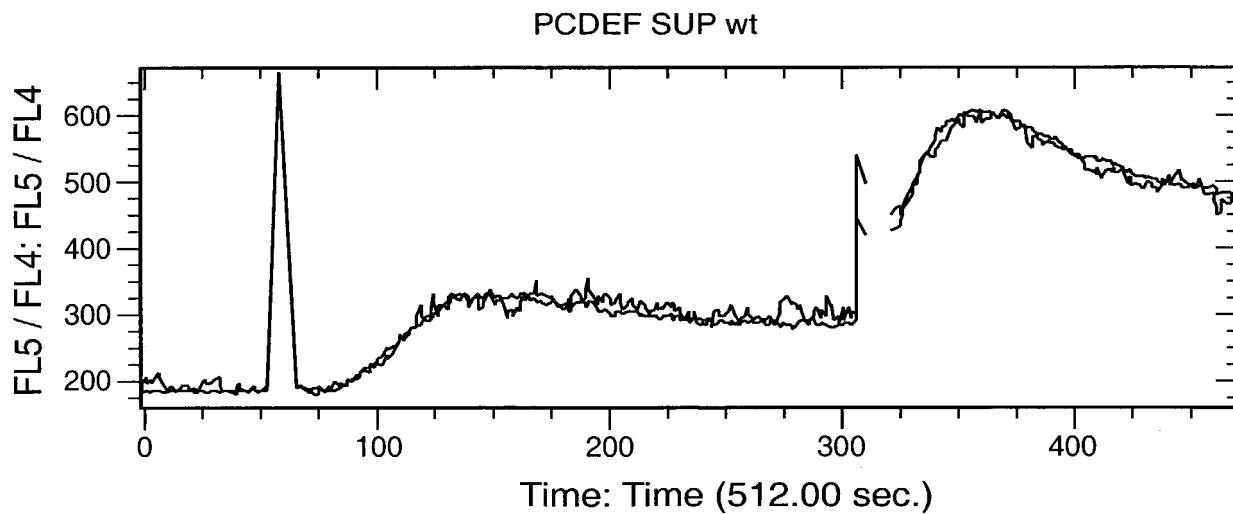


FIG._11K



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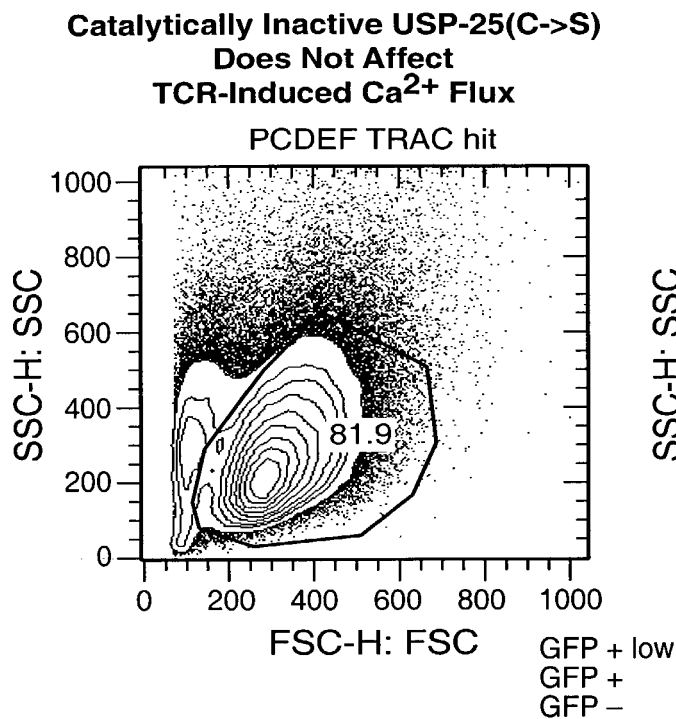


FIG._11L

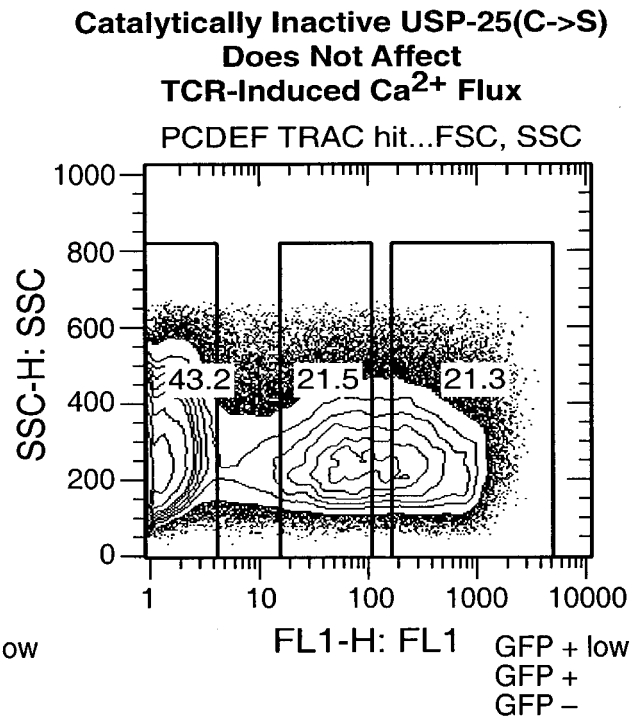


FIG._11M

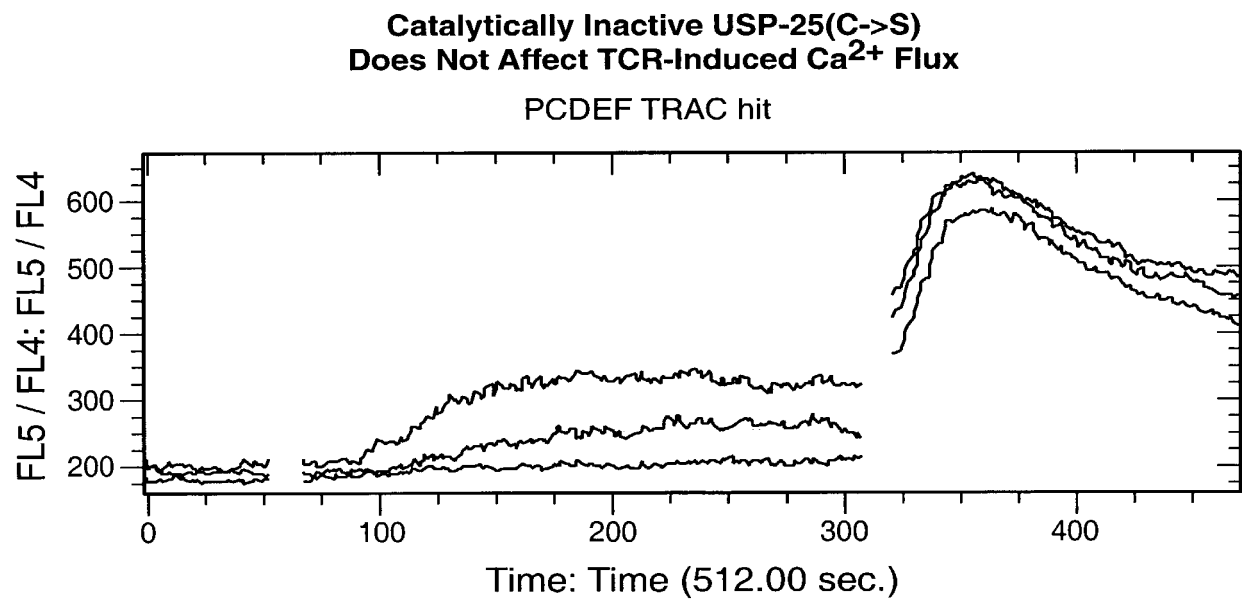


FIG._11N





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USP-25(C->S) Does Not Affect CD69 Expression

Ø C305

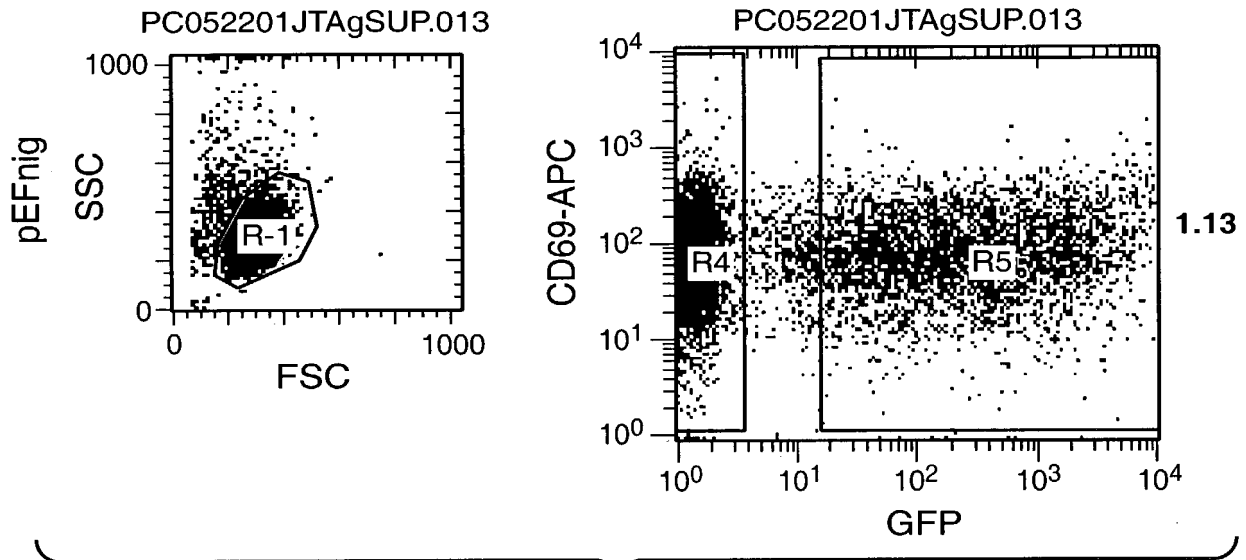


FIG._12A

USP-25(C->S) Does Not Affect CD69 Expression

Ø C305

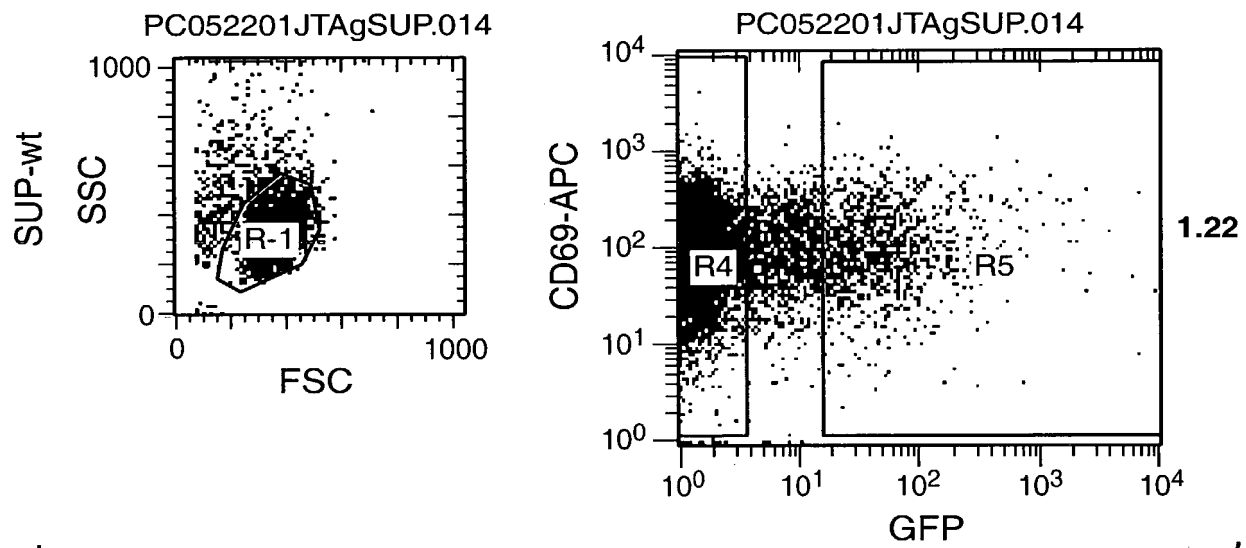


FIG._12B





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USP-25(C->S) Does Not Affect CD69 Expression

Ø C305

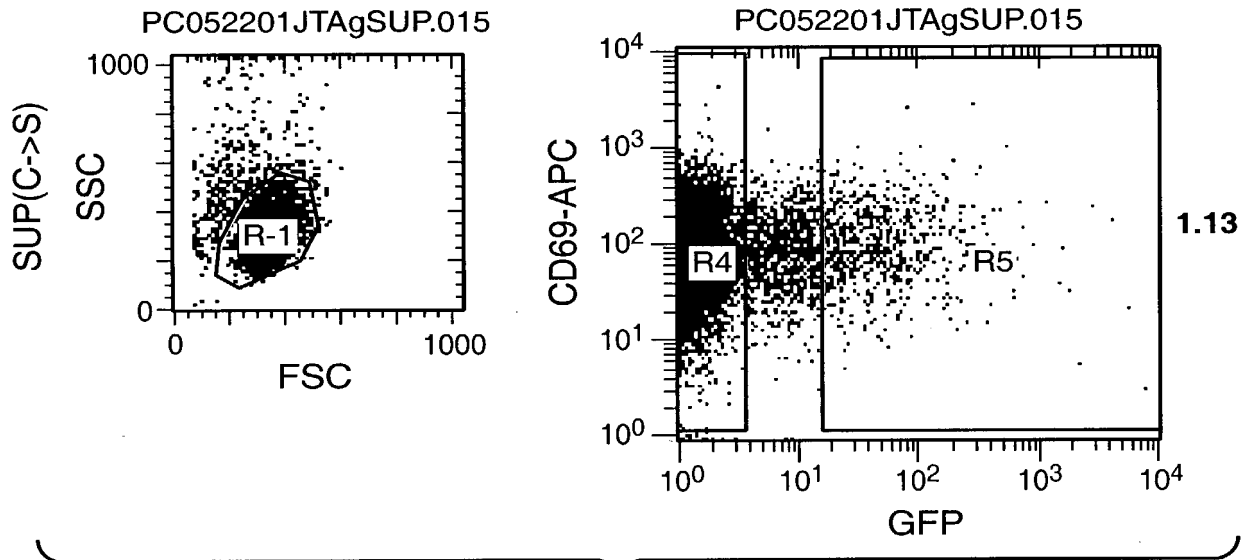


FIG._12C

USP-25(C->S) Does Not Affect CD69 Expression

Ø C305

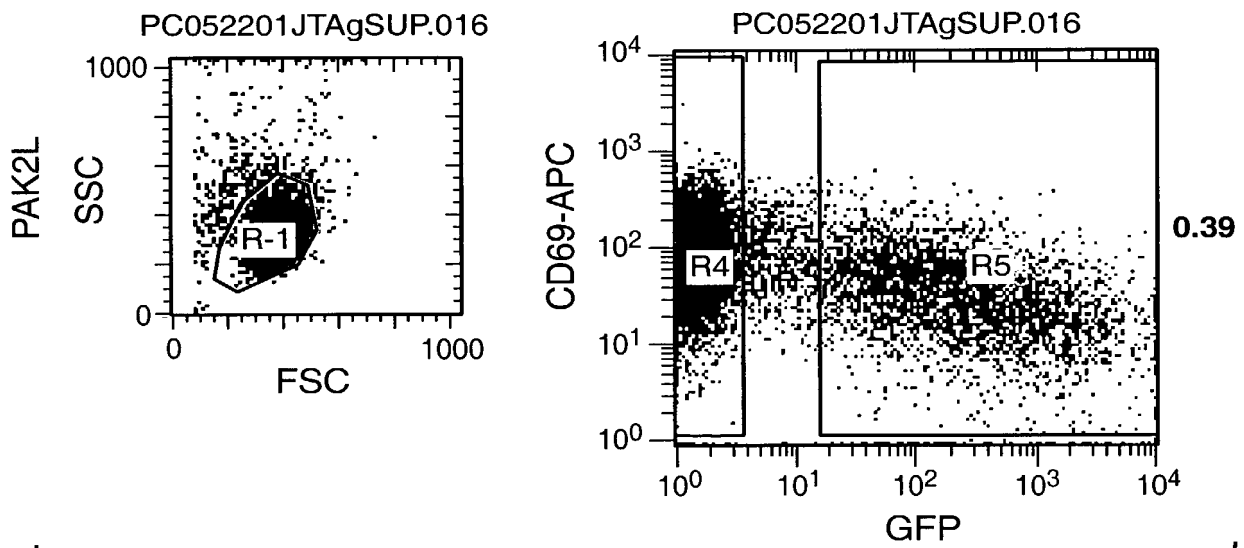


FIG._12D





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USP-25(C->S) Does Not Affect CD69 Expression

+ C305 (100 ng/mL)

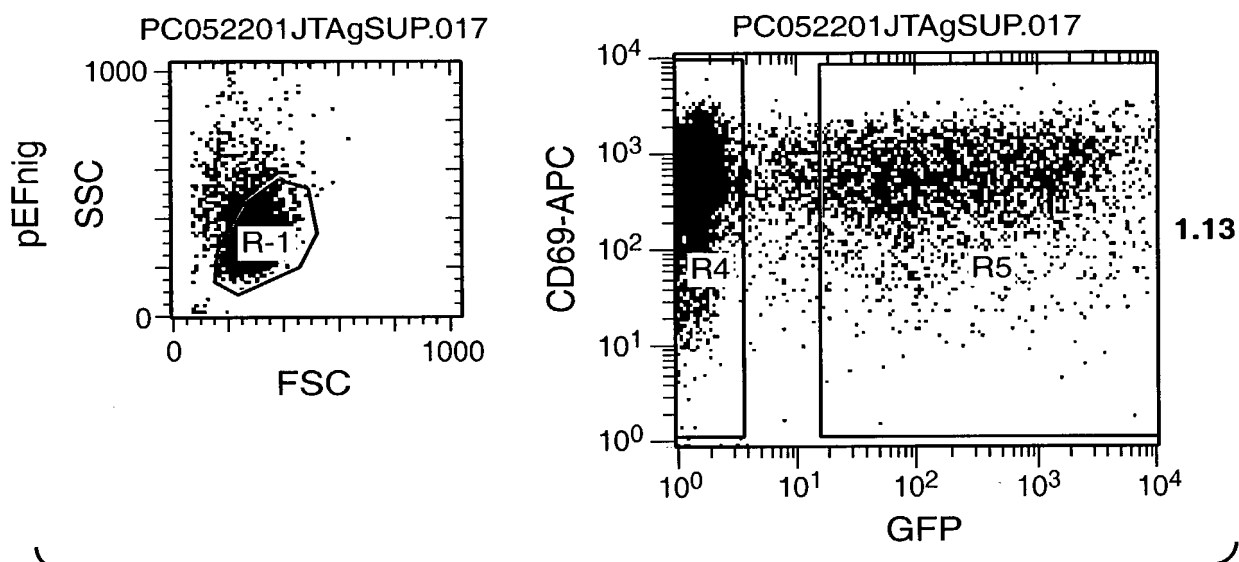


FIG. 12E

USP-25(C->S) Does Not Affect CD69 Expression

+ C305 (100 ng/mL)

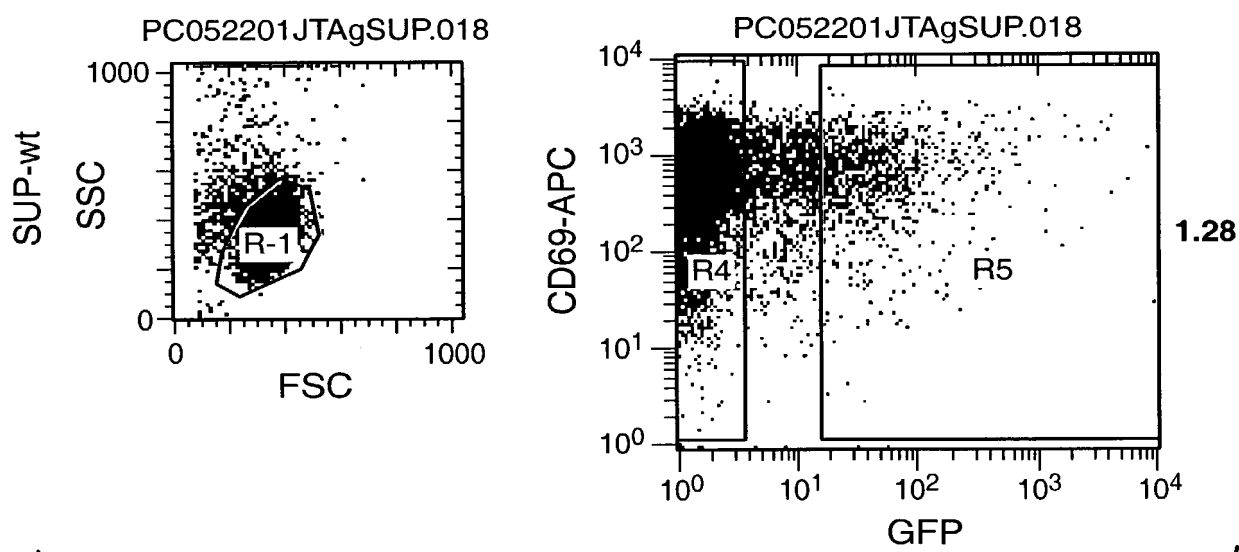


FIG. 12F





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USP-25(C->S) Does Not Affect CD69 Expression

+ C305 (100 ng/mL)

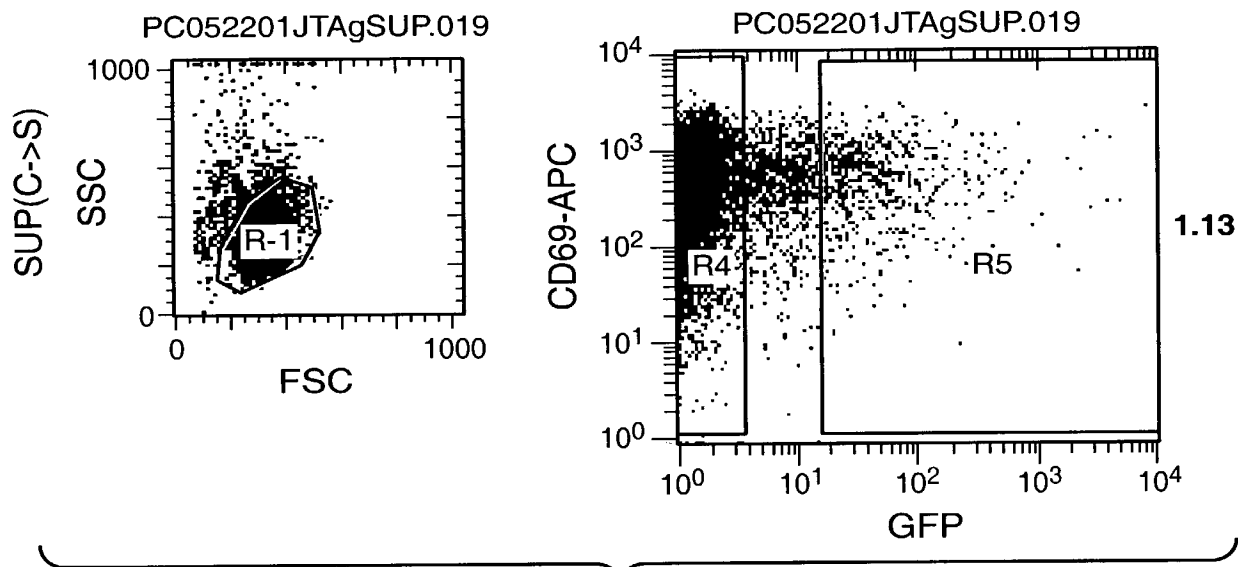


FIG. 12G

USP-25(C->S) Does Not Affect CD69 Expression

+ C305 (100 ng/mL)

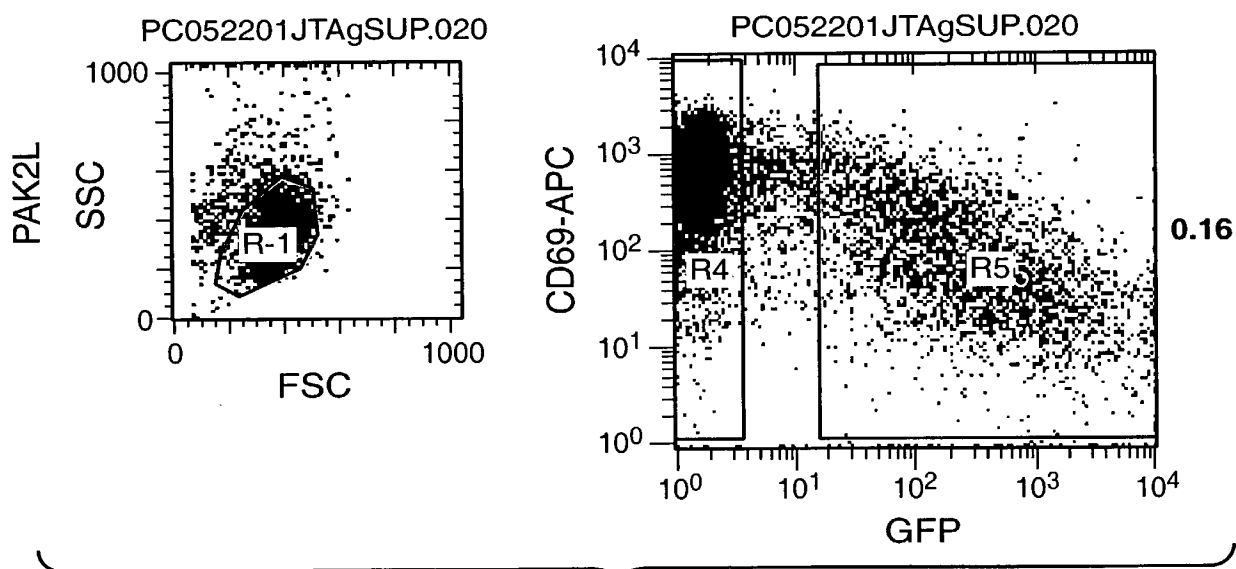


FIG. 12H

+



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USP-25(C->S) Does Not Affect CD69 Expression

+ C305 (300 ng/mL)

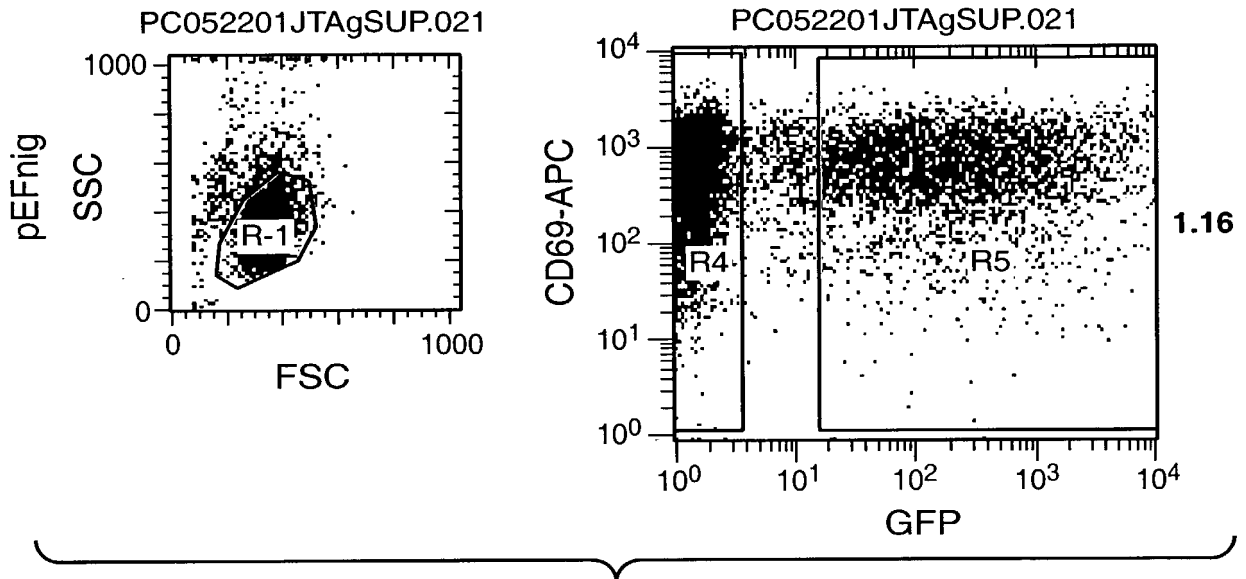


FIG. 12I

USP-25(C->S) Does Not Affect CD69 Expression

+ C305 (300 ng/mL)

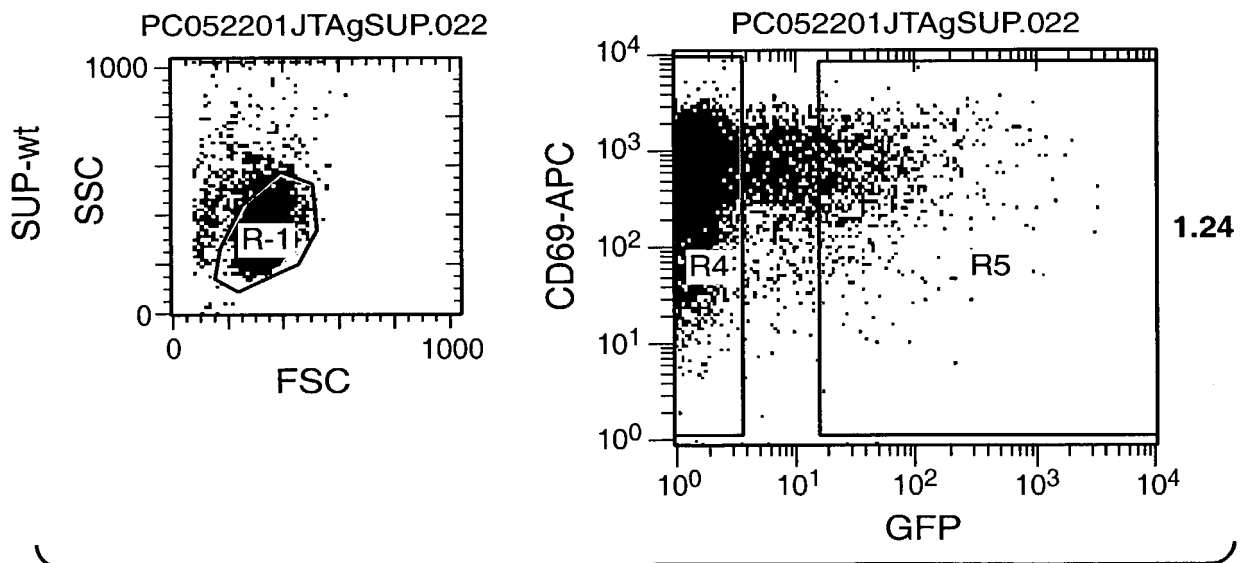


FIG. 12J

+



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USP-25(C->S) Does Not Affect CD69 Expression

+ C305 (300 ng/mL)

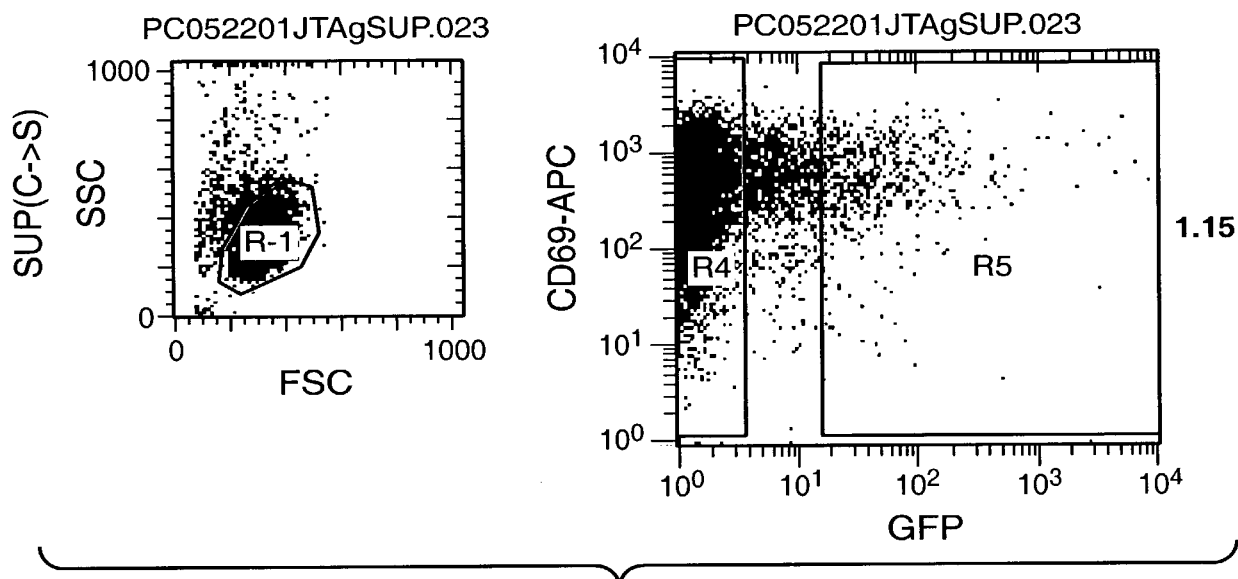


FIG. 12K

USP-25(C->S) Does Not Affect CD69 Expression

+ C305 (300 ng/mL)

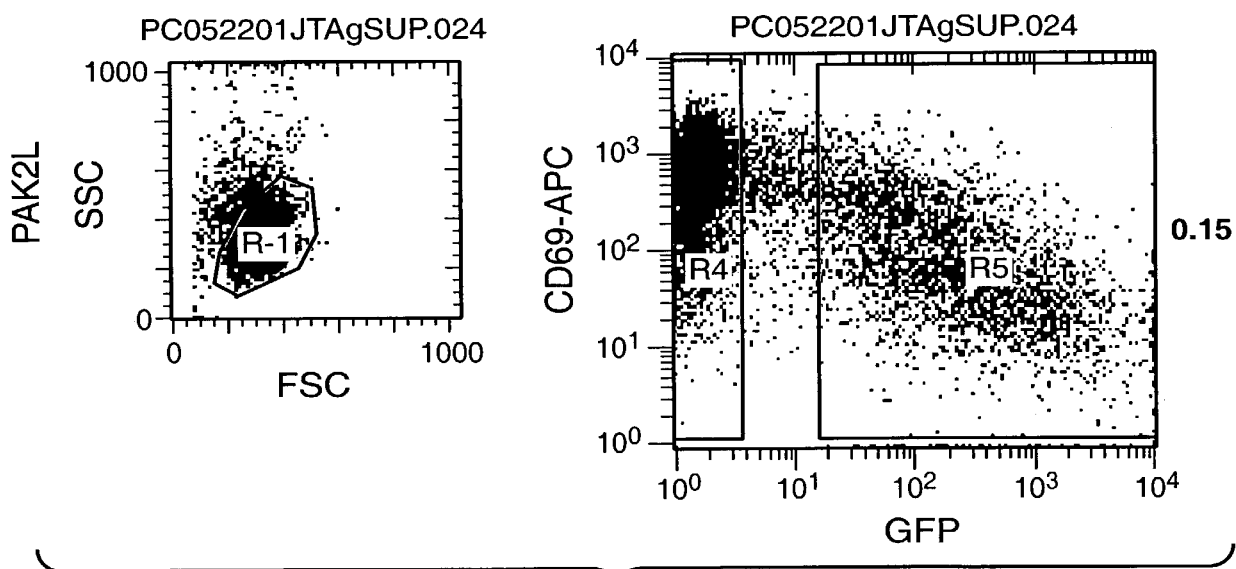


FIG. 12L



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N-Terminal USP-25 Truncation Mutants Inhibit NFAT Activity

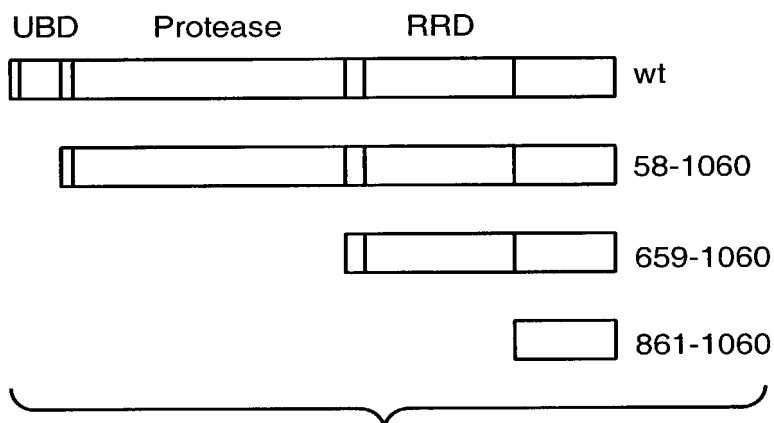


FIG. 12M

N-Terminal USP-25 Truncation Mutants Inhibit NFAT Activity

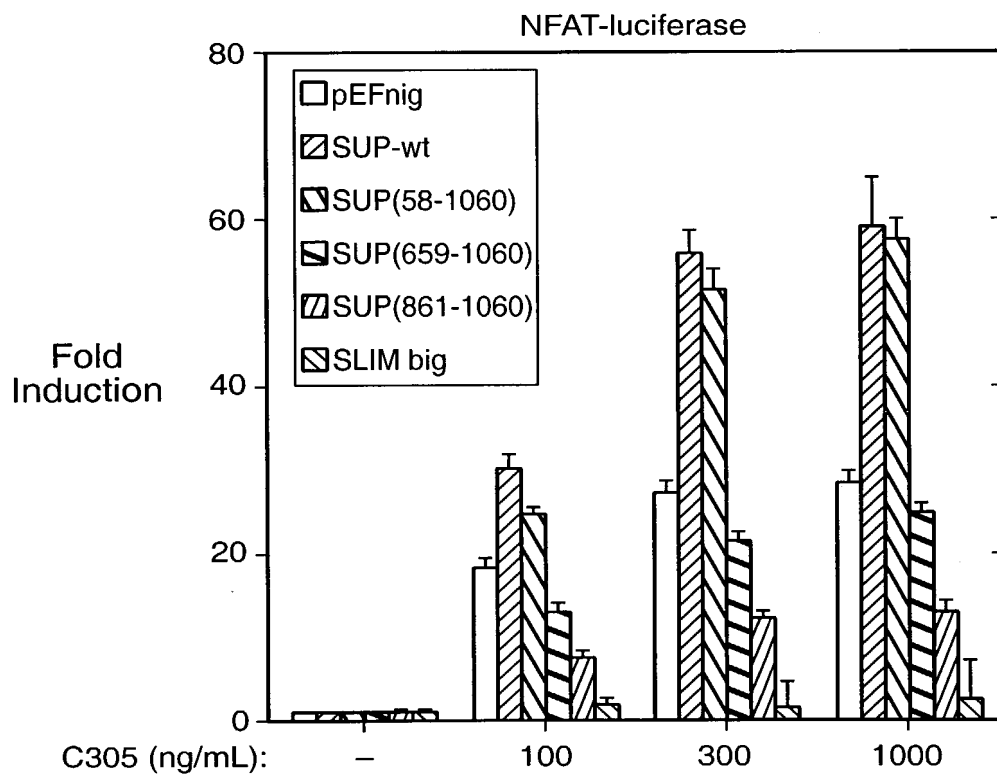


FIG. 12N





USP-25 Mutants Inhibit NFAT Activity in BJABs

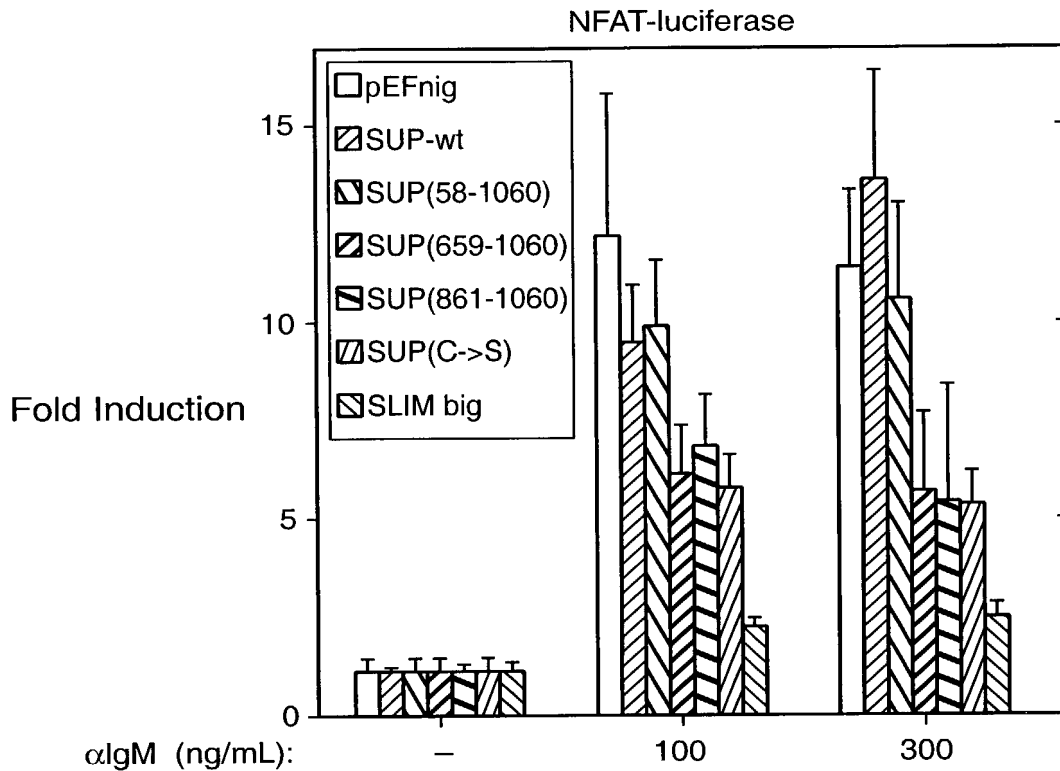


FIG._13A

Possible Regulatory Role of USP-25 on NFAT Activity

- USP-25 Likely Regulates the NFAT Promoter Downstream of Ca^{2+} and Independent of the AP-1 Pathway

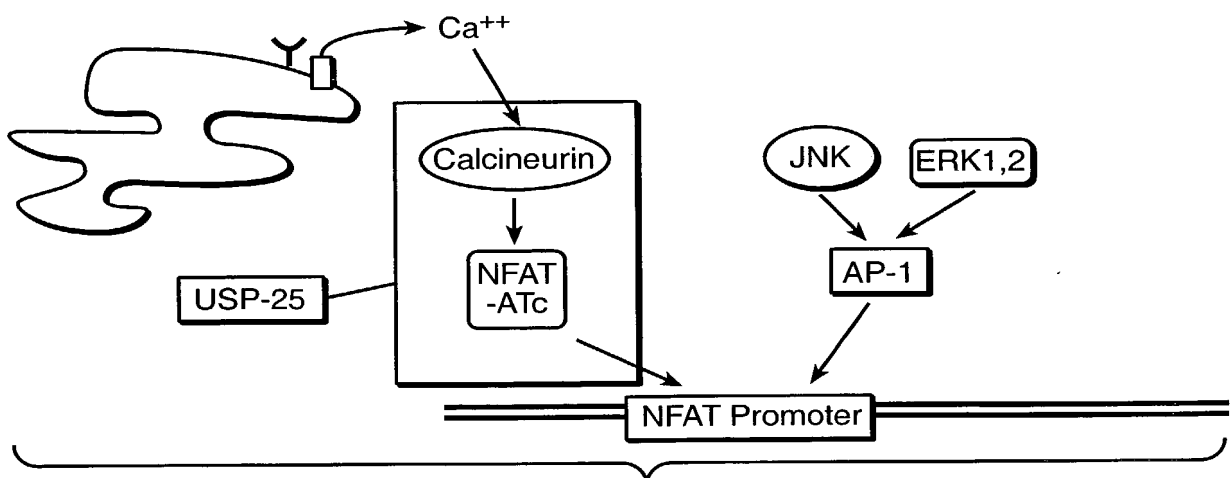


FIG._13B

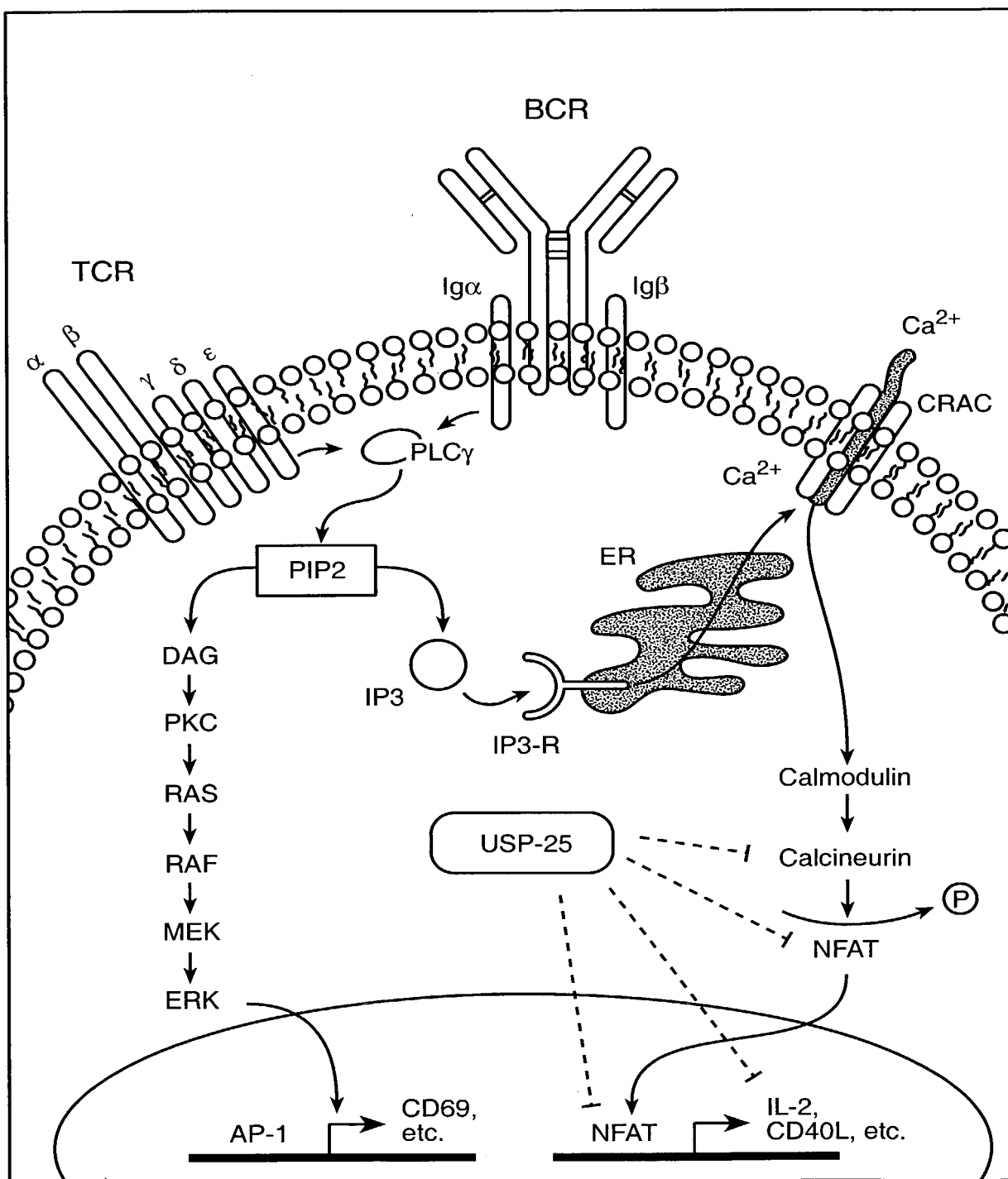


FIG. 14